REMARKS

This is filed in response to the Final Office Action dated January 8, 2007, which rejects claims 1-4, and 6-24.

Amendments to the Claims:

Claims 1-4, and 6-24 have been cancelled. Applicants have added new claims 25-33 of which claim 25 is an independent claim and claims 26-33 depend on claim 25. The new claims embody the subject matter of the cancelled claims but have been re-written to better describe the Applicant's claimed invention and further clarify the scope of the claims. No new subject matter has been added. Support for new claims 25-33 can be found throughout the specification.

Independent claim 25 recites a composition comprising a biocompatible substrate and genetically altered chondrocytes. The genetically altered chondrocytes are modified to express a therapeutic agent and are mixed with the biocompatible substrate to form a mixture. Additionally, the composition allows for the delivery of the therapeutic agent to an atypical chondrocyte environment. Support for the elements of claim 25 can be found in the specification, especially in paragraphs 7, 8, 11, 41, and 82 as well as in examples 5-8 of the application as filed.

Dependent claim 26 recites the composition of claim 25 being further adapted to deliver a therapeutic agent to a target region, and being capable of modifying the one or more cells of the target region. Additionally, claim 27 pertains to using the composition to deliver a therapeutic agent to an environment surrounding a cell associated with a disorder, so as to modify the environment surrounding the cell. Support for the limitations of claims 26 and 27 can be found in paragraphs 9, 13, and 14 of the specification. No new subject matter has been added.

Applicants request the Examiner to enter the new claims and believe that all the new claims are in condition for allowance.

The Applicants Invention:

The instant invention discloses a composition that comprises genetically altered chondrocyte(s) capable of expressing a therapeutic agent in association with a biocompatible substrate. This mixture, when delivered to a target region having one or more cells associated with a disorder, is capable of modifying the one or more cells of the target region. Additionally, the invention also pertains to modifying the environment surrounding a cell associated with a disorder using the genetically altered chondrocyte-biocompatible substrate mixture. Importantly, the instant invention requires that the composition comprising genetically altered chondrocyte and a biocompatible substrate is used to treat disorders in regions that are not associated with chondrocytes i.e., *in atypical chondrocyte environments*. Thus, in order to treat disorders in atypical chondrocyte environments using the claimed composition, it is necessary for the genetically altered chondrocytes to maintain their functional ability to express the therapeutic agent. Neither reference cited as the prior art in the instant office action teach using compositions of genetically altered chondrocyte and biocompatible substrates in the treatment of disorders in atypical chondrocyte environments.

Claim Rejections under 35 USC § 102

Claims 1, 2, 5-14 and 17-24 are rejected by the Examiner under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 6,413,511, (Gloriosos et. al., '511 reference). Additionally, the Examiner has also rejected claims 1-3, and 13-15 under 35 U.S.C. 102(b) as being anticipated by Bartholomew et. al. Applicants have cancelled all the pending claims and have submitted new claims 25-33. The new claims have been re-written to better describe the Applicant's claimed invention and further clarify the scope of the invention. No new subject matter has been added. Applicants believe that the new claims 25-33 represent patentable subject matter in view of both references in the instant office action.

In rejecting the previously pending claims, the Examiner asserted that the '511 reference and the Bartholomew article disclose each and every element of independent claim 1. Applicants respectfully disagree.

The '511 reference teaches a method for introducing a gene of a protein of interest (e.g.: IRAP) into either chondrocytes or synovial cells and the use of such modified cells in *alleviating pathologies of the joint*. The '511 reference is concerned with the treatment of diseased or damaged cartilage tissue using genetically altered chondrocytes and/or altered synovial cells, or the use of genetically altered cells (over-expressing IL-1) to produce animal models for the study of joint pathologies. Although, the '511 reference discloses a composition that has genetically altered chondrocytes mixed with collagen, it only teaches the use of the solidified cell-collagen matrix to repair cartilage tissue by surgically implanting the cell-collagen mixture at the site of repair and the use of fibrin glue to retain the cell-collagen mixture at the surgical site (col. 13, lines 20-24). Stated differently, the '511 reference does not teach or even suggest the use of genetically altered chondrocytes or synovial cells in the treatment of disorders unrelated to joints. New claim 25, however, requires using the altered chondrocytes-biocompatible substrate composition for treating disorders in an atypical chondrocyte environment. To achieve this, the claimed composition must be able to deliver functionally viable genetically altered chondrocytes to an ectopic site, so that the composition allows the proper delivery of the therapeutic agent expressed by the modified chondrocytes within the ectopic environment. The '511 reference thus fails to disclose or teach all the elements of claim 25, and claim 25 is therefore patentable in view of the '511 reference.

The second reference, an article by Bartholomew et. al., evaluates the use of genetically altered human or baboon mesenchymal stem cells (MSC) in gene therapy. Specifically, Bartholomew discloses the use of immunoisolatory devices (IID's) for implanting modified baboon MSC's expressing human EPO into baboons, and the results from in-vitro studies aimed at determining the levels of EPO expressed by genetically modified MSC's in culture. The Bartholomew article also discloses the results of in-vivo experiments aimed at evaluating the serum EPO levels in mice injected with modified human or baboon MSC's or the serum levels of EPO in baboons after implanting immunoisolatory devices containing the modified baboon MSC's.

Bartholomew does not disclose a composition comprising genetically altered chondrocytes and a biocompatible substrate for the treatment of cells associated with a disorder

in a target region. Furthermore, this reference does not even suggest a biocompatible substrate mixed with genetically altered chondrocytes or the use of such a composition to deliver the genetically altered chondrocytes (and the expressed therapeutic agent) to an ectopic environment. The claimed composition distinguishes over this reference since it provides a biocompatible substrate-chondrocyte mixture that can be used for delivery of the chondrocytes to an atypical chondrocytes environment and it further maintains the ability of the altered chondrocytes to express the therapeutic agent within the ectopic environment. New claim 25 is therefore patentable over Bartholomew as well, because this reference does not disclose all the elements of claim 25. Furthermore, Bartholomew does not remedy the deficiencies of the '511 reference. Thus, neither references alone nor in combination teach all the elements of independent claim 25. Claim 25 is therefore patentable over both references.

Claims 26-33 depend on independent claim 25 and incorporate all the limitations of this base claim. These dependent claims are therefore patentable over the cited references for at least the same reasons as claim 25. In addition, at least some of the dependent claims are patentable for reasons other than their dependency on claim 25. Claim 26 recites the composition of claim 25 being further capable of modifying one or more cells associated with a disorder in an atypical chondrocyte environment. Claim 27, claims the composition of claim 25 being adapted to deliver a therapeutic agent to an environment surrounding the cells associated with a disorder, and being capable of modifying said cells. Dependent claim 30 requires that the chondrocytes of the claimed composition have been altered to express a functional erythropoietin mimetibody, while claims 31 and 32 further recite some of the atypical chondrocyte environments to which the claimed composition is delivered. Neither cited reference discloses the erythropoietin mimetibody of new claim 30, nor do the cited references disclose or suggest the atypical chondrocyte environments taught in claims 31 and 32. Applicants believe that new claims 25-33 are therefore in condition for allowance and allowance is respectfully requested.

Claim Rejections under 35 USC § 103(a)

Claims 4 and 16 are rejected by the Examiner under 35 U.S.C. 103(a) as being obvious over Bartholomew et. al., (Human Gene Therapy, 2001, Vol. 12, p 1527-1541). Applicants have cancelled claims 4 and 16. However, the elements of cancelled claim 4 are now found in new

claim 30. As discussed above, Applicants believe that the elements of claim 30 distinguish over the Bartholomew reference.

Claim 30 requires that the chondrocytes of the claimed composition have been altered to express an erythropoietin mimetibody. First, claim 30 depends on new independent claim 25 and therefore incorporates all of its limitations, and as such claim 30 is neither anticipated nor rendered obvious by Bartholomew at. al. Second, Bartholomew discloses delivering the genetically altered mesenchymal stem cells (MSC's), either directly via intra-muscular injection to mice or through the surgical implantation of immunoisolatory devices (IID's) containing the modified MSC's, to baboons. Nowhere does this reference disclose compositions of mixtures of biocompatible substrates and genetically modified cells, or the use of such compositions to express the therapeutic of interest. Bartholomew is concerned with evaluating the use of genetically modified baboon MSC's in gene therapy, particularly, the ability of the modified cells to express hEPO when delivered as an intra-muscular injection or through surgical implantation of the modified cells using immunoisolatory devices. Thus, Bartholomew does not teach the additional elements of claim 30.

Finally, there is no reason to believe that one of ordinary skill in the art would be able to use the teachings of Bartholomew to produce a composition comprising genetically altered chondrocytes and a biocompatible substrate, or the transfection of chondrocytes with a gene for EPO mimetibody. Furthermore, it would not be obvious from the Bartholomew reference to construct such a composition to treat one or more disorders in atypical chondrocyte environments as required by claim 25. Claim 30 is therefore patentable over Bartholomew and allowance is respectfully requested.

Conclusion

Applicants submit that claims 25-33 are allowable, and allowance thereof is respectfully requested. The Examiner is encouraged to telephone the undersigned attorney for Applicants if such communication is deemed necessary to expedite prosecution of this application.

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Respectfully submitted,

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